

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently amended) A method for screening for a bioactive agent ~~capable of modulating~~ that modulates USP-25 protein ubiquitin-specific peptidase activity, comprising:
  - a) combining a USP-25 protein, a USP-25 target protein which is conjugated to ubiquitin ~~or ubiquitin-like protein~~, and a candidate bioactive agent; and
  - b) determining the level of ubiquitin-conjugated ~~or ubiquitin-like protein-conjugated~~ target protein in the presence and absence of said candidate bioactive agent;  
wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to SEQ ID NO:2, wherein said USP-25 protein will bind to said USP-25 target protein, and wherein a difference in the level of ubiquitin-conjugated or ubiquitin-like protein -conjugated target protein in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent ~~is capable of modulating~~ modulates USP-25 protein ubiquitin-specific peptidase activity.
2. (Currently amended) The method according to Claim 1 wherein said USP-25 target protein is selected from the group consisting of UBC9, SYK and calcineurin.
3. (Original) ~~The method according to Claim 1,~~ A method for screening for a bioactive agent that modulates USP-25 protein ubiquitin-like protein specific peptidase activity, comprising:
  - a) combining:  
a USP-25 protein, wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to SEQ ID NO:2, and  
a candidate bioactive agent,

and a USP-25 target protein selected from the group consisting of UBC9, SYK and calcineurin, wherein said USP-25 protein will bind to said USP-25 target protein, and wherein the USP-25 target protein is conjugated to a ubiquitin-like protein, wherein said ubiquitin-like protein is SMT3/SUMO or NEDD8/RUBY; and

b) determining the level of ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent;

wherein a difference in the level of ubiquitin-like protein -conjugated target protein in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent modulates USP-25 protein ubiquitin-like protein specific peptidase activity.

4. (Currently amended) The method according to Claim 1 or claim 3, wherein said USP-25 protein comprises SEQ ID NO:2.

5. (Currently amended) The method according to Claim 1 or claim 3, wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to a fragment of SEQ ID NO:2 wherein said USP-25 protein comprises a ubiquitin-specific peptidase domain.

6. (Withdrawn) A method for screening for a bioactive agent capable of modulating USP-25 protein activity, comprising:

a) combining a USP-25 protein, a USP-25 target protein which is conjugated to ubiquitin or ubiquitin-like protein, and a candidate bioactive agent; and

b) determining the level of ubiquitin-conjugated or ubiquitin-like protein conjugated target protein in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in Figure 4 (SEQ ID NO:4), wherein said USP-25 protein will bind to said USP-25 target protein, and wherein a difference in the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and

absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating USP-25 protein activity.

7. (Withdrawn) The method according to Claim 6, wherein said USP-25 target protein is selected from the group consisting of UBC9, SYK and calcineurin.

8. (Withdrawn) The method according to Claim 6, wherein said ubiquitin-like protein is SMT3/SUMO or NEDD8/RUBY.

9. (Withdrawn) The method according to Claim 6, wherein said USP-25 protein comprises the amino acid sequence set forth in Figure 4 (SEQ ID NO:4).

10. (Withdrawn) The method according to Claim 6, wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to a fragment of the full length amino acid sequence set forth in Figure 4 (SEQ ID NO:4) and wherein said USP-25 protein comprises a ubiquitin-specific peptidase domain.

11. (Currently amended) ~~A The method of claim 1 or 3, for screening for a bioactive agent capable of modulating USP-25 protein activity, comprising:~~

~~a) combining a USP-25 protein, a USP-25 target protein which is conjugated to ubiquitin or ubiquitin-like protein, and a candidate bioactive agent; and~~

~~b) determining the level of ubiquitin-conjugated or ubiquitin-like protein conjugated target protein in the presence and absence of said candidate bioactive agent; wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence is encoded by a nucleic acid sequence with at least 95% identity to SEQ ID NO:1, wherein said USP-25 protein will bind to said USP-25 target protein, and wherein a difference in the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating USP-25 protein activity.~~

12-13. (Cancelled)

14. (Currently amended) The method according to Claim 1 or 11, wherein said USP-25 protein ~~comprises~~ is encoded by SEQ ID NO:1.

15. (Previously presented) The method according to Claim 11, wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to an amino acid sequence encoded by a fragment of SEQ ID NO:1, wherein said USP-25 protein comprises a ubiquitin-specific peptidase domain.

16. (Withdrawn) A method for screening for a bioactive agent capable of modulating USP-25 protein activity, comprising:

a) combining a USP-25 protein, a USP-25 target protein which is conjugated to ubiquitin or ubiquitin like protein, and a candidate bioactive agent; and

b) determining the level of ubiquitin-conjugated or ubiquitin-like protein conjugated target protein in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence encoded by the nucleic acid sequence set forth in Figure 3 (SEQ ID NO:3), wherein said USP-25 protein will bind to said USP-25 target protein, and wherein a difference in the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating USP-25 protein activity.

17. (Withdrawn) The method according to Claim 16, wherein said USP-25 target protein is selected from the group consisting of UBC9, SYK and calcineurin.

18. (Withdrawn) The method according to Claim 16, wherein said ubiquitin-like protein is SMT3/SUMO or NEDD8/RUBY.

19. (Withdrawn) The method according to Claim 16, wherein said USP-25 protein comprises the amino acid sequence encoded by the nucleic acid sequence set forth in Figure 1 (SEQ ID NO:1).

20. (Withdrawn) The method according to Claim 16, wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to an amino acid sequence encoded by a fragment of the full length nucleic acid sequence set forth in Figure 1 (SEQ ID NO:1), wherein said USP-25 protein comprises a ubiquitin-specific peptidase domain.

21. (Withdrawn) A method for screening for a bioactive agent capable of modulating lymphocyte activation, comprising:

- i) contacting a candidate bioactive agent to a lymphocyte comprising a recombinant nucleic acid encoding a USP-25 protein;
- ii) inducing activation of said lymphocyte; and
- iii) determining the activation of said lymphocyte in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in Figure 2 (SEQ ID NO:2), and wherein a difference in the activation of said lymphocyte in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating lymphocyte activation.

22. (Withdrawn) The method according to Claim 21, wherein said USP-25 protein comprises the amino acid sequence set forth in Figure 2 (SEQ ID NO:2).

23. (Withdrawn) The method according to Claim 21, wherein said determining the activation of said lymphocyte comprises determining the activity of the immunoglobulin heavy chain gene promoter or the nuclear factor in activated T cells (NFAT) gene promoter.

24. (Withdrawn) A method for screening for a bioactive agent capable of modulating lymphocyte activation, comprising:

- i) contacting a candidate bioactive agent to a lymphocyte comprising a recombinant nucleic acid encoding a USP-25 protein;

ii) inducing activation of said lymphocyte; and  
iii) determining the activation of said lymphocyte in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in Figure 4 (SEQ ID NO:4), and wherein a difference in the activation of said lymphocyte in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating lymphocyte activation.

25. (Withdrawn) The method according to Claim 24, wherein said USP-25 protein comprises the amino acid sequence set forth in Figure 4 (SEQ ID NO:4).

26. (Withdrawn) The method according to Claim 24, wherein said determining the activation of said lymphocyte comprises determining the activity of the immunoglobulin heavy chain gene promoter or the nuclear factor in activated T cells (NFAT) gene promoter.

27. (Withdrawn) The method according to Claim 23 or 26, wherein said determining the activation of said lymphocyte further comprises determining the expression of CD69.